#### POSSIBLE INTERFERENCE

**DATE:** 2/17/06

TO: BERNHARDT, EMILY, TSANG, CECILIA, WILSON, JAMES

CC: TRUONG, TAMTHOM AND WARD, PAUL

FROM: MCKENZIE, THOMAS C. TCM

**RE**: 09/623,737, 10/623,972, 10/638,848, & 10/817,697

The four cases of concern are 09/623,737 and 10/638,848 both of which are assigned to Examiner Truong, 10/623,972, which is assigned to Examiner Ward, and 10/817,697, which is assigned to me. None of the four applications has issued as a patent although, 10/623,972 and 10/817,697 have been allowed. The claims of 10/623,972 and 10/817,697 are patentably distinct because of differing limitations in radical R¹, the substituent at position 1 of the pyrimidino[4,5-d]pyrimidine ring.

There are no overlapping species among the four cases. There are 53 pyrimidino[4,5-d]pyrimidine species in the two 09/623,737 and 10/638,848 cases. There are 41 pyrimidino[4,5-d]pyrimidine species in the 10/623,972 case. There are 79 pyrimidino[4,5-d]pyrimidine species in the 10/817,697 case. All of the species in the 09/623,737 and 10/638,848 cases either have methyl, ethyl, isopropyl, or cyclopentyl as the substituent at position 1 of the pyrimidino[4,5-d]pyrimidine ring. Thus, none of the species of 09/623,737 and 10/638,848 cases meet the claim limitations of 10/623,972 case, which requires  $C_6H_5$  at this position. None of the species found in the 10/623,972 case fit the claim limitations of 10/638,848 because the closest four species pictured below, have a methoxy group on  $R^3$ , not permitted by the claim limitations in 10/638,848.

There are two species found in the 10/817,697 case which fit the claim limitations of the 10/638,848 case and which are shown below. The first compound pictured below fits the limitations

of claim 1 of 10/638,848 with  $R^1 = (CH_2)_n$ -Ar = 4-fluorophenyl, n = 0,  $R^2 =$  cyclopentyl substituted by OH, and  $R^3 = (CH_2)_n$ -Ar = 4-ethylphenyl, and n = 0. It does not fit the limitations of claim 2 of 10/638,848. There are other close analogues taught in 10/817,697 but all of these have methoxy groups on  $R^3$ , not permitted by the claim limitations of 10/638,848.

There are five species found in the 10/638,848 case which fit the claim limitations of the case 10/817,697 and which are shown below. The first compound pictured below fits the limitations of

claims 1, 3, 12, 13, 16, and 17 of 10/817,697 with  $R^1 = alkyl = methyl$ ,  $R^2 = R^6 = R^7 = R^{10} = R^{12} = H$ ,  $R^3 = COR^{10} = CHO$ ,  $R^4 = R^8 = Cl$ , and  $R^5 = OR^{12}$ . It does not fit the limitations of claims 2, 4-11, 14, 15, 18-24 of 10/817,697.

Listings of the claims and of all the relevant species of cases 10/638,848, 10/623,972, and 10/817,697 are attached.

TCMCK/me

ATTACHMENTS: 6

Day: Friday Date: 2/17/2006 Time: 12:48:27

# **PALM INTRANET**

## Application Number Information

			Examiner <b>TAMTHC</b>	Number: <b>741</b> 4 <u>M</u>	12 / TRUONG	2.		
Filing or 3	Filing or 371(c) Date: <b>08/11/2003</b>			Group Art Unit: 1624 IFW IMAGE				
Effective	Effective Date: 08/11/2003			Class/Subclass: 514/262.100				
Application	on Received: O	8/12/2003	Lost Case	: NO		777		
Pat. Num.	/Pub. Num: / <u>2</u>	0040044012	Interfere	ence Number:	EILE	177		
Issue Dat	te: 00/00/000	00	Unmatche	ed Petition: <b>N</b> O	14			
Date of A	Abandonment:	00/00/0000	<u>L&amp;R Code</u> Code:1	Unmatched Petition: NO  LåR Code: Secrecy Code:1  LAT (53)				
Attorney	Docket Numb	er: <b>5716-</b> D1	Third Lev	el Review: NO	Secrecy Or	der: NO		
Status: 7	1 /RESPONS	E TO NON-F	INAL OFFI	CE ACTION	Status Date	<b>::</b>		
ENTERED	AND FORW	ARDED TO	EXAMINER		10/20/2005	5		
Confirmat	tion Number: 4	1448	Oral Hear	ring: NO				
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DIHYDRO	OPYRIMIDIN	ES AS INHI	BITORS OF	CELLULAR PRO	OLIFERATIO	N		
Bar	PALM	Location	Charge to	Charge to	Employee	Location		
Code	Location	<u>Date</u>	Loc	Name	Name	Locarion		
				= 2				
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Info						39.5		
Search Another: Application# or Patent# Search								
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Day: Friday Date:

## PALM INTRANE

### Application Number Information

Application Number: 09/623737

<u>Assignments</u>

Filing or 371(c) Date: 09/07/2000

Effective Date: 09/07/2000

Application Received: 09/07/2000

Patent Number:

Issue Date: 00/00/0000

Date of Abandonment: 00/00/0000

Attorney Docket Number: 5716-01-

CA

Status: 180 /INTERFERENCE -- DECISION ON PRIORITY

RENDERED BY BOARD OF INTERFERENCES

Confirmation Number: 6362

Oral Hearing: NO Title of Invention: BICYCLIC PYRIMIDINES AND BICYCLIC 3.4-

DIHYDROPYPRIMIDINES AS INHIBITORS OF CELLULAR PROLIFERATION

	2/17/2006
<u> </u>	Time: 12:48:06

Examiner Number:	74142	/ TRUONG,
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TAMTHOM

Group Art Unit: 1624

Class/Subclass: 514/252,160

Lost Case: NO

Interference Number:

104798

Unmatched Petition: NO

L&R Code: Secrecy Code:1

Third Level Review: NO

Status Date:

Secrecy Order: NO

03/31/2004

Bar Code	PALM Location	Location Date	Charge to Loc	Charge to Name	Employee Name	Location
09623737	<u>43C1</u>	06/02/2004	No Charge to Location	No Charge to Name	INVENTORY, FORTY8	

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Search Anoth	ner: Applicat	ion#	or Patent#	මාලෙළි	d l

Day: Friday Date: 2/17/2006 Time: 12:48:06

# **PALM INTRANET**

Application Number Information

Application Number: 09/623737

Examiner Number: 74142 / TRUONG,

**Assignments** 

TAMTHOM

Filing or 371(c) Date: 09/07/2000

Group Art Unit: 1624

Effective Date: 09/07/2000

Class/Subclass: 514/252,160

Application Received: 09/07/2000

Lost Case: NO

Interference Number:

104798

Issue Date: 00/00/0000

Patent Number:

Unmatched Petition: NO

Date of Abandonment: 00/00/0000

L&R Code: Secrecy Code:1

Attorney Docket Number: 5716-01-

Third Level Review: NO

Secrecy Order: NO

CA

Status: 180 /INTERFERENCE -- DECISION ON PRIORITY

Status Date:

RENDERED BY BOARD OF INTERFERENCES

03/31/2004

Confirmation Number: 6362

Oral Hearing: NO

Title of Invention: BICYCLIC PYRIMIDINES AND BICYCLIC 3,4-

DIHYDROPYPRIMIDINES AS INHIBITORS OF CELLULAR PROLIFERATION

Bar Code	PALM Location	Location Date	Charge to Loc	Charge to Name	Employee Name	Location
09623737	<u>43C1</u>	06/02/2004	No Charge to Location	No Charge to Name	INVENTORY, FORTY8	

Appln Contents Petition info . Attylagent info	Continuity Data Foreign Data Inv
Search Another: Application#	or Patent# Search

#### **CLAIMS**

#### What is claimed is:

#### 1. A compound of the formula:

5 wherein:

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 $R^1$  is selected from  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl, or  $C_2$ - $C_{10}$  alkynyl optionally substituted by OH, alkoxy, phenoxy, thio  $C_1$ - $C_{10}$  alkyl, or  $NR^4R^5$ ; (CH<sub>2</sub>)n-Ar, wherein the (CH<sub>2</sub>)<sub>n</sub> alkyl chain is optionally substituted by OH, alkoxy, phenoxy, thio  $C_1$ - $C_{10}$  alkyl, or  $NR^4R^5$ ; COR<sup>4</sup>, wherein  $R^4$  is alkyl optionally substituted by OH, alkoxy, phenoxy, thio  $C_1$ - $C_{10}$  alkyl, or  $NR^4R^5$ ; C<sub>3</sub>- $C_{10}$  cycloalkyl optionally substituted by OH, alkoxy, phenoxy,  $NR^4R^5$ , SO<sub>2</sub> $NR^4R^5$ , or SO<sub>3</sub> $R^4$ ; (CH<sub>2</sub>)<sub>n</sub>heterocyclyl; or alkyl optionally substituted by COR<sup>4</sup>, CO<sub>2</sub> $R^4$  or CONR<sup>4</sup> $R^5$ ;

 $R^4$  is H or  $C_1$ - $C_6$  alkyl;

 $R^5$  is  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $(CH_2)_nAr$ ,  $C_3$ - $C_{10}$  cycloalkyl, heterocyclyl or heteroaryl

n is 0 to 3;

 $R^3$  is  $(CH_2)_nAr$ ;

Ar is phenyl optionally substituted by halo or alkyl optionally substituted by OH, alkoxy, phenoxy, thio  $C_1$ - $C_{10}$  alkyl, or  $NR^4R^5$ ;

R<sup>2</sup> is hydrogen; C<sub>1</sub>-C<sub>10</sub> alkyl substituted by halo, nitrile, OH, alkoxy, phenoxy, thio C<sub>1</sub>-C<sub>10</sub> alkyl, NR<sup>4</sup>R<sup>5</sup> or (CH<sub>2</sub>)-heteroaryl; (CH<sub>2</sub>)<sub>n</sub>Ar, wherein n is 0-3; -(CH<sub>2</sub>)-heteroaryl; C<sub>3</sub>-C<sub>10</sub> cycloalkyl optionally substituted by OH, alkoxy, phenoxy, NR<sup>4</sup>R<sup>5</sup>, SO<sub>2</sub>NR<sup>4</sup>R<sup>5</sup>, or SO<sub>3</sub>R<sup>4</sup>; (CH<sub>2</sub>)-heterocyclyl; or COR<sup>4</sup>;

 $R^4$  is H,  $C_1$ - $C_6$  alkyl optionally substituted by halogen;  $NR^5R^6$ ; cycloalkyl; or (CH<sub>2</sub>)-Ar;

 $R^5$  and  $R^6$  are independently  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $(CH_2)_nAr$ ,  $C_3$ - $C_{10}$  cycloalkyl, heterocyclyl or heteroaryl; or a pharmaceutically acceptable salt form thereof.

- 2. A compound of Claim 1 wherein  $R^3$  is  $(CH_2)_nAr$  substituted by one or two halogens.
- 3. A compound of Claim 1 wherein R<sup>2</sup> is hydrogen; C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted by halo, nitrile, OH, alkoxy, phenoxy, thio C<sub>1</sub>-C<sub>10</sub> alkyl, NR<sup>4</sup>R<sup>5</sup> or (CH<sub>2</sub>)-heteroaryl.
- 4. A method for the preparation of a compound of Claim 1, said method comprising:
  - (a) treating a compound of the formula:

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wherein L is a leaving group, with an amine of the formula  $R^1$ -NH<sub>2</sub>, wherein n,  $R^1$ ,  $R^2$  and  $R^3$  have the meanings provided in Claim 1.

- 5. A method for the preparation of a compound of Claim 1, said method comprising:
- 25 (a) treating a compound of the formula:

with an oxidizing agent followed by an amine of the formula  $R^1$ -NH<sub>2</sub>, wherein n,  $R^1$ ,  $R^2$  and  $R^3$  have the meanings provided in Claim 1.

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6. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of Claim 1 and a pharmaceutically acceptable carrier.

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=> 10/638,848 compounds

L7 ANSWER 1 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

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L7 ANSWER 2 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

$$\begin{array}{c|c} & i - Pr & & & \\ & \downarrow & & \\ O & N & N & \\ & N & N & \\ & & N & \\ & & & N & \\ & & N & \\$$

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 3 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

$$\begin{array}{c} \text{i-Pr} \\ \text{O} \\ \text{N} \\ \text{O} \\ \text{O} \\ \text{N} \\$$

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 4 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 5 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 6 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 7 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

L7 ANSWER 8 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 9 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

$$\begin{array}{c|c} \text{Et}_2\text{N-} \text{(CH}_2)_3\text{-NH} & \text{OMe} \\ \hline \\ \text{N} & \text{N} & \text{OMe} \\ \end{array}$$

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 10 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

L7 ANSWER 11 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 12 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

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L7 ANSWER 13 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

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L7 ANSWER 15 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

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L7 ANSWER 16 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 18 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 19 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

$$Me$$

$$NH \qquad N \qquad N \qquad N \qquad O \qquad C1$$

$$C1$$

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L7 ANSWER 22 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

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L7 ANSWER 26 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

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L7 ANSWER 27 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

L7 ANSWER 28 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 29 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 30 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

Thomas McKenzie

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L7 ANSWER 31 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

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L7 ANSWER 33 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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L7 ANSWER 35 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 36 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

10/470,974 Page 13

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 37 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 38 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 39 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

$$\begin{array}{c|c} \text{Et}_2\text{N-} (\text{CH}_2)_4 - \text{NH} & \text{N} & \text{O} & \text{Me} \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & \\ & \\ & & \\ & \\ & & \\ & & \\ & \\ & \\ & & \\ & \\ & \\ & \\ & & \\ & \\ & \\ & \\ & \\ & \\ & \\$$

L7 ANSWER 40 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

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L7 ANSWER 41 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 42 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

$$\begin{array}{c|c} \text{Et}_{2}\text{N}-\left(\text{CH}_{2}\right)_{4}-\text{NH} & \\ \text{N} & \\ \text{N} & \\ \text{N} & \\ \text{OMe} \end{array}$$

10/470,974

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 43 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 44 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 45 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

L7 ANSWER 46 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 47 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 48 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

L7 ANSWER 49 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 50 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 51 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

L7 ANSWER 52 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

$$\begin{array}{c|c} & & & \\ &$$

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L7 ANSWER 53 OF 53 REGISTRY COPYRIGHT 2006 ACS on STN

Day: Friday Date: 2/17/2006 Time: 12:57:11

IFW IMAGE

Query Request

Mail N/=.

Status Date:

01/04/2006

Desc.

Waiting for Response

Secrecy Order: NO

## **PALM INTRANET**

### Application Number Information

Application Nu	mber: 10	1623972
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**Assignments** 

Filing or 371(c) Date: 07/21/2003

Effective Date: 07/21/2003

Application Received: 07/22/2003

Pat. Num./Pub. Num: /20040038995

Issue Date: 00/00/0000

Date of Abandonment: 00/00/0000

Examiner Number: 80316 / WARD, PAUL

Group Art Unit: 1623

Class/Subclass:

544/256,000 Lost Case: NO

Interference Number:

Unmatched Petition: NO

L&R Code: Secrecy

Code:1

Attorney Docket Number: 21266 US1 Third Level Review: NO

Status: 94 /PUBLICATIONS -- ISSUE FEE PAYMENT

RECEIVED

Confirmation Number: 5346  Oral Hearing: NO  Fitle of Invention: PYRIMIDO COMPOUNDS HAVING ANTIPROLIFERATIVE  ACTIVITY  L9 (41)						NEST Y	
Bar Code	PALM Location	Location Date	Charge to Loc	Charge to Name	Employee Name	Location	
10623972IW	<u>7410</u>	01/04/2006	No Charge to Location	No Charge to Name	BABAAN, NOEL	IDC/01/	

ppln Contents Petition Info Atty/Agent Info	Continuity Data	Foreign Data   Inv
Search Another: Application# Search	or Patent#	Search
PCT / Searce	or PG PUBS #	<b>‡</b>

### IN THE CLAIMS

1. (Currently amended) A co

A compound of formula:

I,

wherein

R1 is selected from the group

-H.

-COR4, and

-COOCHR®OCOR®;

R<sup>2</sup> and R<sup>3</sup> are independently selected from

-H, and

-OR5;

R<sup>4</sup> is selected from the group

-C1-8 alkyl,

-lower alkyl substituted by up to 4 groups independently selected from

-NR<sup>5</sup>R<sup>6</sup>,

-SR5,

-OR5,

- -aryi,
- -aryl substituted by up to 2 groups independently selected from
- -OR<sup>5</sup> and C<sub>1-4</sub> lower alkyl, and
- -heteroaryl, and
- -heterocycle;

R<sup>5</sup> and R<sup>6</sup> are independently selected from

- -H, and
- C<sub>1-5</sub> lower alkyl,

or, alternatively, -NR<sup>5</sup>R<sup>8</sup> can form a ring having 3 to 7 atoms, said ring optionally including one or more additional N or O atoms;

### or the pharmaceutically acceptable salts thereof.

- 2. (Original) The compound of claim 1 wherein R<sup>1</sup> is -COR<sup>4</sup>.
- 3. (Original) The compound of claim 2 wherein R<sup>2</sup> is H.
- 4. (Original) The compound of claim 3 wherein R<sup>3</sup> is H.
- 5. (Previously presented) The compound of claim 4 which is selected from the group:

N-[3-(4-Methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-N-phenylacetamide;

*N*-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-*N*-phenylpropanamide;

- 2-Amino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimldino[4,5-d]pyrimidin-7-yl)]-N-phenylacetamide acetic acid salt;
- 2-Amino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-N-phenylacetamide hydrochloric acid salt;
- (2S)-2-Amino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-4-methylthio-N-phenylbutanamide;
- (2S)-2-amino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-4-methylthio-N-phenylbutanamide acetic acid salt;
- (2S)-2-Amino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-4-methylthio-N-phenylbutanamide hydrochloric acid sait;
- (2S)-2-Amino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrlmidino[4,5-d]pyrimidin-7-yl)]-3-phenyl-N-phenylpropanamide;
- (2S)-2-Amino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-3-phenyl-N-phenylpropanamide hydrochloric acid salt;
- (2S)-2-Amino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-4-methyl-N-phenylpentanamide acetic acid salt;
- (2S)-2-Amino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-4-methyl-N-phenylpentanamide hydrochloric acid salt;
- (2S)-2-Amino-3-(4-hydroxyphenyl)-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-N-phenylpropanamide hydrochloric acid salt;

- (2S)-2,6-Diamino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-N-phenylhexanamide di-hydrochloric acid salt;
- (2S)-2-Amlno-3-indol-3-yl-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-N-phenylpropanamide hydrochloric acid salt;
- (2S)-2-Amino-3-hydroxy-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-N-phenylpropanamide;
- (2R)-2-Amino-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrlmidino[4,5-d]pyrimidin-7-yl)]-4-methylthio-N-phenylbutanamide hydrochloric acid salt;
- *N*-[3-(4-Methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-*N*-phenylpentanamide; and
- N-[3-(4-Methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimldin-7-yl)]-N-phenylbutanamide.
- 6. (Previously presented) The compound of claim 2 which is selected from the group:
- N-(4-Hydroxyphenyl)-N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]acetamide; and
- *N*-(4-methoxyphenyl)-*N*-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]acetamide.
  - 7. (Original) The compound of claim 1 wherein R<sup>1</sup> Is -COOCHR<sup>5</sup>OCOR<sup>4</sup>.
  - 8. (Original) The compound of claim 7 wherein  $R^2$  is H.

- 9. (Original) The compound of claim 8 wherein R<sup>3</sup> is H.
- 10. (Previously presented) The compound of claim 9 which is selected from the group:

{N-[3-(4-Methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)}- N-phenylcarbamoyloxy}methyl acetate;

{*N*-[3-(4-Methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-*N*-phenylcarbamoyloxy}methyl 2-(dimethylamino)acetate;

{N-[3-(4-Methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)}- N-phenylcarbamoyloxy}methyl 2-(dimethylamino)acetate hydrochloric acid salt; and

{N-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yl)]-N-phenylcarbamoyloxy}methyl piperidine-4-carboxylate trifluoroacetic acid salt.

- 11. (Original) The compound of claim 1 wherein R¹ is H.
- 12. (Original) The compound of claim 11 wherein R<sup>2</sup> is H.
- 13. (Previously presented) The compound of claim 12 which is selected from the group:

3-(4-Methoxyphenyl)-1-phenyl-7-(phenylamino)-1,3,4-trihydropyrimidino[4,5-d]pyrimidin-2-one;

3-(4-Methoxyphenyl)-1-phenyl-7-(phenylamino)-1,3,4-trihydropyrimldino[4,5-d]pyrimidin-2-one methanesulfonate salt:

7-[(4-Hydroxyphenyl)amino]-3-(4-methoxyphenyl)-1-phenyl-1,3,4-trihydropyrimidino[4,5-d]pyrimldln-2-one; and

3-(4-Methoxyphenyl)-7-[(4-methoxyphenyl)amino]-1-phenyl-1,3,4-trihydropyrimidino[4,5-d]pyrimidin-2-one.

14. (Original) A compound selected from the group:

3-(4-Methoxyphenyl)-1-phenyl-7-(phenylamino)-1,3,4-trihydropyrimidino[4,5-d]pyrimidin-2-one.

3-(4-Methoxyphenyl)-1-phenyl-7-(phenylamino)-1,3,4-trihydropyrimidino[4,5-d]pyrimidin-2-one methanesulfonate salt,

7-[(4-Hydroxyphenyl)amino]-3-(4-methoxyphenyl)-1-phenyl-1,3,4-trihydropyrimidino[4,5-d]pyrimidin-2-one, and

3-(4-Methoxyphenyl)-7-[(4-methoxyphenyl)amino]-1-phenyl-1,3,4-trihydropyrimidino[4,5-d]pyrimidin-2-one.

15. (Original) A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and pharmaceutically acceptable carrier or exciplent.

Claim 16. (Canceled).

Claim 17. (Canceled).

NO. 2833 P. 9

Serial No. 10/623,972 Filed: July 21, 2003

18. (Previously presented) A method of-treating lung, colon or prostate cancer comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.

Claim 19. (Cancelled).

20. (Previously presented) A compound selected from the group:

(Chloromethoxy)-*N*-[3-(4-methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimidin-7-yi)]-*N*-benzamide,

3-(4-Methoxyphenyl)-1-phenyl-7-{[4-(1,1,2,2-tetramethyl-1-silapropoxy) phenyl]amino}1,3,4-trihydropyrimidino[4,5-d]pyrimidin-2-one, and

N-[3-(4-Methoxyphenyl)-2-oxo-1-phenyl(1,3,4-trihydropyrimidino[4,5-d]pyrimldin-7-yl)]-N-[4-(1,1,2,2-tetramethyl-1-silapropoxy)phenyl]acetamide.

>=> 10/623,972 compounds

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L9 ANSWER 2 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L9 ANSWER 3 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L9 ANSWER 4 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L9 ANSWER 5 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L9 ANSWER 6 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L9 ANSWER 7 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L9 ANSWER 8 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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L9 ANSWER 9 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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- L9 ANSWER 12 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN

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- L9 ANSWER 13 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN

- \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*
- L9 ANSWER 14 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

● HCl

L9 ANSWER 15 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

● HCl

L9 ANSWER 16 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN CM 1

Absolute stereochemistry.

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CM 2

L9 ANSWER 17 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

● HCl

L9 ANSWER 18 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L9 ANSWER 19 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

● HCl

L9 ANSWER 20 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN CM 1

Absolute stereochemistry.

CM 2

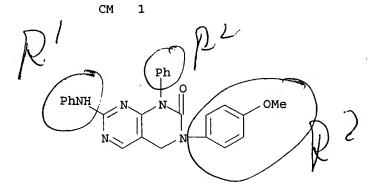
L9 ANSWER 21 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN

HCl

L9 ANSWER 22 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN

● HCl

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CM 1

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L9 ANSWER 31 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

● HCl

L9 ANSWER 32 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN Absolute stereochemistry.

● HCl

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●2 HCl

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● HCl

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L9 ANSWER 36 OF 41 REGISTRY COPYRIGHT 2006 ACS on STN CM 1

CM 2

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Desc.

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Waiting for Response

Secrecy Order: NO

Status Date:

02/06/2006

E-278-> F48

Examiner Number: 77575 / MCKENZIE,

## **PALM INTRANET**

Application Number Information

Application Number: 10/817697

**Assignments** 

Filing or 371(c) Date: 04/02/2004

Effective Date: 04/02/2004

Application Received: 04/05/2004

Pat. Num./Pub. Num: /20040204427

Issue Date: 00/00/0000

Date of Abandonment: 00/00/0000

Attorney Docket Number: 21635US1

Status: 93 /NOTICE OF ALLOWANCE MAILED --

APPLICATION RECEIVED IN OFFICE OF PUBLICATIONS

Confirmation Number: 3178

Oral Hearing: NO

Title of Invention: PYRIMIDO COMPOUNDS HAVING ANTIPROLIFERATIVE

THOMAS

Group Art Unit: 1624

Interference Number:

L&R Code: Secrecy

Unmatched Petition: NO

Third Level Review: NO

Class/Subclass:

544/256,000

Lost Case: NO

Code:1

Bar Code	PALM Location	Location Date	Charge to Loc	Charge to Name	Employee Name	Location
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This listing of the claims will replace all prior versions and listings of the claims in this application.

## In the Claims:

1. (Currently amended) A compound of formula

$$\begin{array}{c|c}
R^8 & R^7 \\
R^6 & R^5 \\
R^2 & R^3 & R^6
\end{array}$$

wherein

R<sup>1</sup> is selected from the group consisting of

- -H,
- -(CH<sub>2</sub>)<sub>n</sub>-heterocycle,
- -lower alkyl substituted by up to three groups selected from -OR<sup>9</sup>, -COR<sup>10</sup>, -CO<sub>2</sub>R<sup>10</sup>, -CONR<sup>10</sup>R<sup>11</sup>, -SO<sub>2</sub>NR<sup>10</sup>R<sup>11</sup>, SO<sub>2</sub>R<sup>10</sup> or -CN;
- -cycloalkyl,
- -alkenyl, and
- -alkynyl,

where n is 0, 1, 2, or 3, and the heterocycle, alkyl, cycloalkyl, alkenyl, and alkynyl groups are each independently, optionally substituted by up to 3 groups selected from

Serial No. 10/817,697 Filed: April 2, 2004 -OR<sup>9</sup>, -COR<sup>10</sup>. -CO<sub>2</sub>R<sup>10</sup>, -CONR<sup>10</sup>R<sup>11</sup>, -SO<sub>2</sub>NR<sup>10</sup>R<sup>11</sup>, -SO₂R<sup>10</sup>, and -CN; R<sup>2</sup> and R<sup>3</sup> are independently selected from the group consisting of -H, -OR<sup>9</sup>, -halogen, -COR<sup>10</sup>, -CO<sub>2</sub>R<sup>40</sup>, -(CH<sub>2</sub>)<sub>n</sub>-heterocycle, -alkyi, -cycloalkyl, -alkenyl, and -alkynyl, where n is 0, 1, 2, or 3, and the heterocycle, alkyl, cycloalkyl, alkenyl, and alkynyl groups are each independently, optionally substituted by up to 3 groups selected from -OR<sup>9</sup>.

- -OR<sup>9</sup>,
  -halogen,
  -COR<sup>10</sup>, and
  -CO<sub>2</sub>R<sup>10</sup>;
- $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$  and  $R^8$  are each independently selected from the group consisting of -H,
  - -lower alkyl that optionally may be substituted by hydroxy or alkoxy,

Serial No. 10/817,697 Filed: April 2, 2004 -OR<sup>12</sup>, -halogen,

R<sup>9</sup> is selected from the group consisting of

-H,

-COR<sup>10</sup>.

-COR<sup>13</sup>, and

-CO<sub>2</sub>R<sup>13</sup>;

-lower alkyl that optionally may be substituted by hydroxy or alkoxy,

-cycloalkyl that optionally may be substituted by hydroxy, alkoxy, and lower alkyl, and

-heterocycle that optionally may be substituted by hydroxy, alkoxy or lower alkyl;

R<sup>10</sup> and R<sup>11</sup> are each independently selected from the group consisting of -H.

-lower alkyl that optionally may be substituted by hydroxy or alkoxy,

-cycloalkyl that optionally may be substituted by hydroxy, alkoxy or lower alkyl, and

-heterocycle that optionally may be substituted by hydroxy, alkoxy or lower alkyl;

R<sup>12</sup> is selected from the group consisting of -H, lower alkyl and -COR<sup>13</sup>; and

R<sup>13</sup> is selected from the group consisting of -H and lower alkyl;

or the pharmaceutically acceptable salts thereof.

- 2. (Currently amended) The compound of claim 1 wherein R<sup>1</sup> is selected from cycloalkyl; cycloaklyl substituted by –OH; heterocycle; <del>lower-alkyl;</del> and lower alkyl substituted by –OH.
  - 3. (Original) The compound of claim 1 wherein R<sup>2</sup> is -H or -OCH<sub>3</sub>.
  - 4. (Original) The compound of claim 1 wherein R<sup>3</sup> is -H, F, or -OCH<sub>3</sub>.
  - 5. (Original) The compound of claim 1 wherein R<sup>2</sup> and R<sup>3</sup> are both -H.
  - 6. (Original) The compound of claim 1 wherein R<sup>4</sup>, R<sup>5</sup> and R<sup>7</sup> are -H.
  - 7. (Original) The compound of claim 1 wherein R<sup>6</sup> is halogen or OR<sup>12</sup>.
  - 8. (Original) The compound of claim 7 wherein R<sup>6</sup> is -OCH<sub>3</sub>.
  - 9. (Original) The compound of claim 1 wherein R<sup>8</sup> is -H or -F.
- 10. (Original) The compound of claim 1 wherein R<sup>9</sup> is -H, lower alkyl, or lower alkyl substituted by hydroxy.
  - 11. (Original) The compound of claim 10 wherein R<sup>9</sup> is -H.
- 12. (Original) The compound of claim 1 wherein R<sup>10</sup> is -H, lower alkyl, or lower alkyl substituted by hydroxy.
  - 13. (Original) The compound of claim 12 wherein R<sup>10</sup> is -H.
- 14. (Original) The compound of claim 1 wherein R<sup>11</sup> is -H, lower alkyl, or lower alkyl substituted by hydroxy.

- 15. (Original) The compound of claim 14 wherein R<sup>11</sup> is -H.
- 16. (Original) The compound of claim 1 wherein R<sup>12</sup> is -H or lower alkyl.
- 17. (Original) The compound of claim 16 wherein R<sup>12</sup> is -H.
- 18. (Original) The compound of claim 1 wherein R<sup>13</sup> is -H or lower alkyl.
- 19. (Original) The compound of claim 18 wherein R<sup>13</sup> is -H.
- 20. (Currently amended) A compound selected from the group:
- 1-Cyclohexyl-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one(Example 1e),
- 3-(4-Methoxy-phenyl)-7-phenylamino-1-piperidin-4-yl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one(Example 2b),
- 1-(*trans*-4-Hydroxy-cyclohexyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one(Example 3c),
- 3-(4-Methoxy-phenyl)-7-phenylamino-1-piperidin-3-yl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one(Example 4b),
- 1-Cyclopentyl-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one(Example 5),
- 1-(1,1-Dioxo-tetrahydro-1I 6-thiophen-3-yl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one(Example-6),
- 3-[3-(4-Methoxy-phenyl)-2-oxo-7-phenylamino-3,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-1-yl]-piperidine-1-carbaldehyde(Example-7),
- 3-(4-Methoxy-phenyl)-7-phenylamino-1-(tetrahydro-pyran-4-yl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one(Example-8),
- (±)-1-(*trans*-3-Hydroxy-cyclopentyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 9d), and

- ( $\pm$ )-cis-1-(3-Hydroxy-cyclopentyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one(Example 10e).
  - 21. (Currently amended) A compound selected from the group:
- (*R*)-3-(4-Methoxy-phenyl)-7-phenylamino-1-(tetrahydro-furan-3-yl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 11b) (*R*)-3-(4-Methoxy-phenyl)-7-phenylamino-1-pyrrolidin-3-yl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one(Example 12).
- ( $\pm$ )-7-(4-Fluoro-phenylamino)-1-(trans-3-hydroxy-cyclopentyl)-3-(4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 13c),
- ( $\pm$ )-3-(2-Fluoro-4-methoxy-phenyl)-1-(trans-3-hydroxy-cyclopentyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 14d),
- (S)-(+)-1-(2-Hydroxy-1-methyl-ethyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 15d),
- (S)-(+)-7-(4-Fluoro-phenylamino)-1-(2-hydroxy-1-methyl-ethyl)-3-(4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 16),
- 3-(2-Fluoro-4-methoxy-phenyl)-1-(*trans*-4-hydroxy-cyclohexyl)-7-(4-methoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 17d),
- 3-(2-Fluoro-4-methoxy-phenyl)-1-(*trans*-4-hydroxy-cyclohexyl)-7-(3,4-dimethoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 18),
- 3-(4-Methoxy-phenyl)-1-(*trans*-4-hydroxy-cyclohexyl)-7-(3,4-dimethoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 19c),
- 3-(4-Methoxy-phenyl)-1-(*trans*-4-hydroxy-cyclohexyl)-7-(4-methoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 20b), and
- (S)-(+)-3-(2-Fluoro-4-methoxy-phenyl)-7-(4-fluoro-phenylamino)-1-(2-hydroxy-1-methylethyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 21b).
  - 22. (Currently amended) A compound selected from the group:
- (S)-(+)-3-(2-Fluoro-4-methoxy-phenyl)-1-(2-hydroxy-1-methyl-ethyl)-7-(4-methoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 22),

- (R)-(-)-1-(2-Hydroxy-1-methyl-ethyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example-23d),
- 3-(4-Methoxy-phenyl)-1-methyl -7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidine-2-one-(Example-24b),
- 1-(2-methoxy-ethoxymethyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 25),
- 3-[-3-(4-Methoxy-phenyl)-2-oxo-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-1-yl]-propionitrile-(Example 26),
- (+)-(1*R*,3*R*)-1-(3-Hydroxy-cyclopentyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 27f),
- (R)-1-(2-Hydroxy-propyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 28d),
- (-)-(1*S*,3*S*)-1-(3-Hydroxy-cyclopentyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 29h),
- 3-[-3-(4-Methoxy-phenyl)-2-oxo-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-1-yl]-propionamide (Example-30), and
- (S)-(+)-1-(2-Hydroxy-propyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 31d).
  - 23. (Currently amended) A compound selected from the group:
- 1-(*cis*-3,5-Dihydroxy-cyclohexyl)-3-(2-fluoro-4-methoxy-phenyl)-7-(4-methoxyphenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 32f),
- 1-(*cis*-3,5-Dihydroxy-cyclohexyl)-3-(4-methoxy-phenyl)-7-(4-methoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 33c),
- 1-(cis-3,5-Dihydroxy-cyclohexyl)-3-(4-methoxy-phenyl)-7-(4-fluoro-3-methoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 34f),
- 1-(cis-3,5-Dihydroxy-cyclohexyl)-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 35b),
- 1-(cis-3,5-Dihydroxy-cyclohexyl)-3-(2-fluoro-4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 36b),

1-(*cis*-3,5-Dihydroxy-cyclohexyl)-3-(2-fluoro-4-methoxy-phenyl)-7-(4-fluoro-3-methoxyphenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 37b),

(R)-3-(4-Ethyl-phenyl)-7-(4-fluoro-phenylamino)-1-(2-hydroxy-1-methyl-ethyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 38g),

( $\pm$ )-3-(4-Ethyl-phenyl)-7-(4-fluoro-phenylamino)-1-(trans-3-hydroxy-cyclopentyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 39d), and

1-Cyclopropylmethyl-3-(4-methoxy-phenyl)- 7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidine-2-one (Example 40).

## 24. (Original) A compound of formula

$$R^8$$
 $R^7$ 
 $R^6$ 
 $R^8$ 
 $R^7$ 
 $R^6$ 
 $R^5$ 
 $R^2$ 
 $R^3$ 

wherein

R1 is selected from

-H,

-lower alkyl substituted by -OH, COR<sup>10</sup>, -CN or -CONH<sub>2</sub>,

-(CH<sub>2</sub>)<sub>n</sub>-heterocycle,

-(CH<sub>2</sub>)<sub>n</sub>-heterocycle substituted by -COR<sup>10</sup>, -CO<sub>2</sub>R<sup>10</sup> or (=O)<sub>2</sub>,

cycloalkyl,

cycloalkyl substituted by -OH;

R<sup>2</sup> is H or -OCH<sub>3</sub>;

R<sup>3</sup> is H, F or -OCH<sub>3</sub>;

R<sup>4</sup>, R<sup>5</sup> and R<sup>7</sup> are H;
R<sup>6</sup> is –OCH<sub>3</sub> or lower alkyl;
R<sup>8</sup> is H or F H;
R<sup>10</sup> is lower alkyl substituted by alkoxy; and n is 0 or 1.

- 25. (Original) A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and pharmaceutically acceptable carrier or excipient.
- 26. (Currently amended) A method for treating <u>breast</u>, <u>lung</u>, <u>colon or prostate</u> cancer comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.
- 27. (Currently amended) A method of controlling <u>breast</u>, <u>lung</u>, <u>colon or prostate</u> cancer comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.
- 28. Cancelled.
- 29. Cancelled.
- 30. (Currently amended) A compound selected from the group:
- 4-[3-(4-Methoxy-phenyl)-2-oxo-7-phenylamino-3,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-1-yl]-piperidine-1-carboxylic acid *tert*-butyl ester-(Example-2a),
- 1-[trans-4-(tert-Butyl-dimethyl-silanyloxy)-cyclohexyl]-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example-3b),

- 3-[3-(4-Methoxy-phenyl)-2-oxo-7-phenylamino-3,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-1-yl]-piperidine-1-carboxylic acid *tert*-butyl ester-(Example 4a),
- (±)-3-cis-(tert-Butyl-dimethyl-silanyloxy)-cyclopentyl]-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 10d),
- (R)-2-Methylsulfanyl-4-(tetrahydro-furan-3-ylamino)-pyrimidine-5-carboxylic acid ethyl ester-(Example 11a),
- (±)-4-[trans-3-(tert-Butyl-dimethyl-silanyloxy)-cyclopentylamino]-2-methylsulfanyl-pyrimidine-5-carbaldehyde-(Example 13a),
- (±)-1-[trans-3-(tert-Butyl-dimethyl-silanyloxy)-cyclopentyl]-3-(4-methoxy-phenyl)-7-methylsulfanyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example-13b),
- (±)-[3-trans-(tert-Butyl-dimethyl-silanyloxy)-cyclopentyl]-{5-[(2-fluoro-4-methoxy-phenylamino)-methyl]-2-methylsulfanyl-pyrimidin-4-yl}-amine (Example 14b),
- ( $\pm$ )-1-[trans-3-(tert-Butyl-dimethyl-silanyloxy)-cyclopentyl]-3-(4-methoxy-phenyl)-7-methylsulfanyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example-14c),
- (S)-1-[2-(*tert*-Butyl-diphenyl-silanyloxy)-1-methyl-ethyl]-7-chloro-3-(4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 15c),
- 1-[trans-4-(tert-Butyl-dimethyl-silanyloxy)-cyclohexyl]-7-chloro-3-(2-fluoro-4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 17c),
- 1-[trans-4-(tert-Butyl-dimethyl-silanyloxy)-cyclohexyl]-7-chloro-3-(4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 19a),
- 1-[*trans-*4-(*tert*-Butyl-dimethyl-silanyloxy)-cyclohexyl]-3-(4-methoxy-phenyl)-7-(3,4-dimethoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 19b), and
- 1-[trans-4-(tert-Butyl-dimethyl-silanyloxy)-cyclohexyl]-3-(4-methoxy-phenyl)-7-(4-methoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 20a).
  - 31. (Currently amended) A compound selected from the group:
- (S)-1-[2-(*tert*-Butyl-diphenyl-silanyloxy)-1-methyl-ethyl]-7-chloro-3-(2-fluoro-4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 21a),

- (R)-1-[2-(tert-Butyl-diphenyl-silanyloxy)-1-methyl-ethyl]-7-chloro-3-(4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 23c),
- 3-(4-Methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidine-2-one (Example-24a).
- (+)-(1R,3R)-4-[3-(tert-Butyl-dimethyl-silanyloxy)-cyclopentylamino]-2-methylsulfanyl-pyrimidine-5-carboxylic acid ethyl ester-(Example 27d),
- (-)-(1*R*,3*R*)-1-[3-(*tert*-Butyl-dimethyl-silanyloxy)-cyclopentyl]-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 27e),
- (R)-1-[2-(tert-Butyl-diphenyl-silanyloxy)-propyl]-7-chloro-3-(4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 28c),
- (-)-(1*S*,3*S*)-4-[3-(*tert*-Butyl-dimethyl-silanyloxy)-cyclopentylamino]-2-methylsulfanyl-pyrimidine-5-carboxylic acid ethyl ester-(Example 29d),
- (-)-(1S,3S)-4-[3-(*tert*-Butyl-dimethyl-silanyloxy)-cyclopentylamino]-2-methylsulfanyl-pyrimidine-5-carbaldehyde (Example 29e),
- (-)-(1*S*,3*S*)-1-[3-(*tert*-Butyl-dimethyl-silanyloxy)-cyclopentyl]-3-(4-methoxy-phenyl)-7-methylsulfanyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 29f),
- (-)-(1S,3S)-1-[3-(*tert*-Butyl-dimethyl-silanyloxy)-cyclopentyl]-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example-29g),
- (S)-1-[2-(*tert*-Butyl-diphenyl-silanyloxy)-propyl]-7-chloro-3-(4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 31c),
- 1-[cis-3,5-Bis-(tert-butyl-diphenyl-silanyloxy)-cyclohexyl]-7-chloro-3-(2-fluoro-4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 32d),
- 1-[cis-3,5-Bis-(tert-butyl-diphenyl-silanyloxy)-cyclohexyl]-3-(2-fluoro-4-methoxy-phenyl)-7-(4-methoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 32e), and
- 1-[cis-3,5-Bis-(tert-butyl-diphenyl-silanyloxy)-cyclohexyl]-7-chloro-3-(4-methoxy-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 33a).
  - 32. (Currently amended) A compound selected from the group:
- 1-[cis-3,5-Bis-(tert-butyl-diphenyl-silanyloxy)-cyclohexyl]-3-(4-methoxy-phenyl)-7-(4-methoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example-33b),

- 1-[cis-3,5-Bis-(tert-butyl-diphenyl-silanyloxy)-cyclohexyl]-3-(4-methoxy-phenyl)-7-(4-fluoro-3-methoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 34e),
- 1-[cis-3,5-Bis-(tert-butyl-diphenyl-silanyloxy)-cyclohexyl]-3-(4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 35a),
- 1-[cis-3,5-Bis-(tert-butyl-diphenyl-silanyloxy)-cyclohexyl]-3-(2-fluoro-4-methoxy-phenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example-36a),
- 1-[cis-3,5-Bis-(tert-butyl-diphenyl-silanyloxy)-cyclohexyl]-3-(2-fluoro-4-methoxy-phenyl)-7-(4-fluoro-3-methoxy-phenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 37a),
- (2,4-Dichloro-pyrimidin-5-ylmethyl)-(4-ethyl-phenyl)-amine (Example 38c),
- (R)-3-[2-(tert-Butyl-dimethyl-silanyloxy)-1-methyl-ethyl]-1-(2,4-dichloro-pyrimidin-5-ylmethyl)-1-(4-ethyl-phenyl)-urea-(Example-38d),
- (R)-1-[2-(tert-Butyl-dimethyl-silanyloxy)-1-methyl-ethyl]-7-chloro-3-(4-ethyl-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 38e),
- (R)-1-[2-(*tert*-Butyl-dimethyl-silanyloxy)-1-methyl-ethyl]-3-(4-ethyl-phenyl)-7-(4-fluorophenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example 38f),
- (±)-[trans-3-(tert-Butyl-dimethyl-silanyloxy)-cyclopentyl]-{2-chloro-5-[(4-ethyl-phenylamino)-methyl]-pyrimidin-4-yl}-amine-(Example 39a),
- (±)-1-[trans-3-(tert-Butyl-dimethyl-silanyloxy)-cyclopentyl]-7-chloro-3-(4-ethyl-phenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one (Example 39b), and
- (±)-1-[trans-3-(tert-Butyl-dimethyl-silanyloxy)-cyclopentyl]-3-(4-ethyl-phenyl)-7-(4-fluorophenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one-(Example-39c).

=> 10/817,697 compounds

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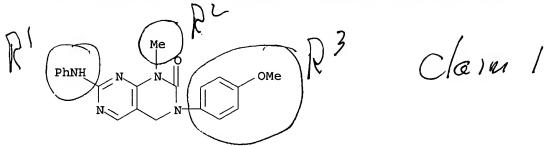
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Absolute stereochemistry. Rotation (-).

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Relative stereochemistry.

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Relative stereochemistry.

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